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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,350	08/24/2000	Klaus Cichutek	11692-004001	3834

7590

07/13/2004

Fish & Richardson  
225 Franklin Street  
Boston, MA 02110-2804

EXAMINER

WINKLER, ULRIKE

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/555,350	<b>Applicant(s)</b> CICHUTEK ET AL.	
	<b>Examiner</b> Ulrike Winkler	<b>Art Unit</b> 1648	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 23 April 2004.  
2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-9, 19 and 20 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
5) ☒ Claim(s) 9 and 19 is/are allowed.  
6) ☒ Claim(s) 1-8 and 20 is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.  
10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All    b) ☐ Some \*    c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

The Amendment filed April 24, 2004 in response to the Office Action of October, 21, 2003 is acknowledged and has been entered. Claims 1-9, 19 and 20 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

#### *Claim Rejections - 35 USC § 103*

The rejection of claims 1-8 and 20 under 35 U.S.C. 103(a) as being unpatentable over Dornburg (U.S. Pat No. 5,869,331), Novotny et al. (in Molecular Biology and Biotechnology, 1995), Colcher et al. (Journal of the National Cancer Institute, 1990) and June et al. (U.S. Pat. No. 6,352,694 et al.) **is maintained** for reasons of record.

Applicant's arguments have been fully considered but they fail to persuade. Applicant's arguments are that there is no motivation to combine the references and that the references do not teach all of the claim limitations.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. *In re McLaughlin*, 170 USPQ 209 (CCPA 1971).

In response to applicant's argument that there is no suggestion to combine the

Art Unit: 1648

references, the examiner recognizes that references cannot be arbitrarily combined and that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references. *In re Nomiya*, 184 USPQ 607 (CCPA 1975). However, there is no requirement that a motivation to make the modification be expressly articulated. The test for combining references is what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. *In re McLaughlin*, 170 USPQ 209 (CCPA 1971). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. *In re Bozek*, 163 USPQ 545 (CCPA 1969).

In this case, Dornburg teaches retroviral vector particles having altered target cell specificity because the retroviral particles has a single chain antibody molecule fused with the viral envelope protein. These antibody envelope fusion particles were infection competent (see column 10, lines 10-15). The retroviral particle of the reference uses the peptide antigen binding sites directed against the cell surface molecule of the target cell (see claims 1-5). The reference teaches that in order to alter the host range of the retroviral particle the envelope protein may be modified with a protein that recognizes cell surface structures, antibodies are proteins that are able to do this (see column 4, lines 25-35). The reference teaches inserting the single chain antibody molecule into an envelope expression vector (see column 7, lines 30-65), the expression vector is inserted into a helper cell (for purpose of packaging) and the particles were used in infectivity assays (see column 9, lines 20-25). The reference does not teach the production of an antibody against a cell surface molecule using as the starting material a whole cell immunogen.

Art Unit: 1648

June et al. teach various production methods for generating antibodies to cell surface molecules, the immunogen may be a purified protein or alternatively may simple be a whole cell which expresses the surface protein of interest (see columns 21 and 22, especially column 22, lines 56-58). The reference also sets out the production of combinatorial antibodies (see column 26-27) from B-cell pools derived from immunized animals. The reference teaches expressing the antibody library on a filamentous phage which can then be used for screening purposes (see column 27, lines 38-45). Therefore, the reference teaches the production of an antibody against a cell surface protein using a whole cell immunogen as the starting point. The reference also teaches using a filamentous phage display as a means of screening for desirable antibody binding, these nucleic acids encoding the selected antibodies can be subcloned into other expression vectors using standard recombinant techniques (column 27, lines 37-45). The reference teaches claim limitations a-f.

Colcher et al. teaches that the Mab B6.2 IgG, used by Dornburg above, was generated by the immunization of Balb/c mice with membrane-enriched fraction of a human breast tumor (see material and methods).

Novotny et al. teaches that the standard step required for the production of single chain antibodies has become a standard technique in the art. The figure discloses that the rearranged V genes are amplified using PCR, IgG mRNA can be used to obtain the post immunization repertoire.

It would have been obvious to one of ordinary skill in the art to make a cell specific retroviral vector using a single chain antibody following the steps of Dornburg. Dornburg teaches that in order to change the target cell specificity of the virus requires

Art Unit: 1648

the insertion of a single chain antibody molecule that can recognize a cell surface marker on the target cell. One having ordinary skill in the art at the time the invention was made would have been motivated to use whole cells for the immunization step in animals because the use of whole cells requires less preparation of the antigen, additionally, June et al. expressly teaches the use of whole cell as an immunogen in animals. One having ordinary skill in the art at the time would also recognize that injecting a whole cell in the animal allows for the production of antibodies that recognize not only the cell surface receptors but also see the receptor in context of other cell surface molecules, this is also taught by the June et al reference. Combining the teaching of Dornburg and June et al. the ordinary artisan would have been motivated to start with whole cell immunogen to produce antibodies that can then be used to alter viral target cell specificity. Therefore, the instant invention is obvious over Dornburg (U.S. Pat No. 5,869,331), Novotny et al. (in Molecular Biology and Biotechnology, 1995), Colcher et al. (Journal of the National Cancer Institute, 1990) and June et al. (U.S. Pat. No. 6,352,694 et al.).

### ***Conclusion***

Claims 9 and 19 are allowable, SEQ ID NO: 1 is free of the prior art of record.

Claims 1-8 and 20 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Art Unit: 1648

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


Papers related this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989). The Group 1600 Official Fax number is: (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [[ulrike.winkler@uspto.gov](mailto:ulrike.winkler@uspto.gov)].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.

  
ULRIKE WINKLER, PH.D.  
PRIMARY EXAMINER

7/12/04